

### ABSTRACT OF THE DISCLOSURE

Methods of using a heme-deficient mutant sGC with a substituted His105 residue, which has a high basal specific activity and displays properties similar to NO-stimulated wild type sGC, are disclosed. Preferred embodiments aid in the prevention and treatment of cyclic GMP-dependent pathophysiologies, and are useful in the development of drugs that inhibit or activate sGC. Certain embodiments provide a method of treating angina and other chronic heart diseases comprising delivery of a constitutively active  $\alpha\beta^{\text{Cys105}}$  mutant gene or enzyme to an *in vivo* cell are described.